COMPETITIVE NMDA RECEPTOR ANTAGONISTS AND AGONIST: EFFECTS ON SPONTANEOUS ALTERNATION IN MICE EXPOSED TO CEREBRAL OLIGEMIA

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The purpose of the present study was to investigate the effects of competitive NMDA receptor antagonists, D.L-(E)-2-amino-4-methyl-5-phosphono-3-pentenoic acid (CGP 37849) and its ethyl ester (CGP 39551), or agonist, N-methyl-D-aspartate (NMDA) on spontaneous alternation in mice exposed to cerebral oligemia. Alternation behavior was evaluated in an Y-maze. Transient cerebral oligemic hypoxia was induced by bilateral clamping of carotid arteries (BCCA) for 30 min under pentobarbital anesthesia. In BCCA mice, CGP 37849 (5 mg/kg, ip) impaired spontaneous alternation when given 48 h or 7 days after surgery. CGP 39551 (5 mg/kg, ip) had no effect. NMDA (50 mg/kg, sc) improved performance of the task in BCCA mice when tested 48 h after surgery.

These results suggest that cerebral oligemic hypoxia induced by BCCA leads to functional disturbances in the central nervous system, such as spontaneous alternation impairment and increased susceptibility to NMDA receptor-related drugs. Adverse potential of cerebral oligemia may limit a therapeutic use of NMDA receptor antagonists.

Key words: CGP 37849, CGP 39551, NMDA, cerebral oligemic hypoxia, spontaneous alternation

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